Review

Imaging swallowing function and the mechanisms driving dysphagia in inclusion body myositis

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Received on December 23, 2023; accepted in revised form on February 9, 2024.

Clin Exp Rheumatol 2024; 42: 425-435.

Key words: dysphagia, imaging, inclusion body myositis, pathophysiology

Competing interests: see page 433.

ABSTRACT

Sporadic inclusion body myositis (IBM) is a progressive condition which commonly affects patients aged above 40. IBM does not respond to immunosuppression and no proven treatments are available.

Up to 80% of patients develop some degree of swallowing impairment during the disease course. Dysphagia is a source of marked morbidity in IBM and predisposes patients to life-threatening complications such as aspiration pneumonia. The pathophysiology behind dysphagia in IBM is not fully understood. Evidence from imaging demonstrates that impaired swallowing is predominantly underpinned by oropharyngeal deficits. Changes in cricopharyngeal physiology is thought to be an important factor influencing dysphagia in IBM. However, it is unclear whether this is secondary to structural changes within the cricopharyngeus itself or driven by impairment of the muscles promoting pharyngeal clearance.

The approach to dysphagia in IBM patients is limited by a lack of validated instruments to reliably assess swallowing function and an absence of effective therapeutic interventions derived from controlled trials targeting dysphagia.

Imaging modalities such as the video fluoroscopic swallowing study (VFSS) are commonly used to evaluate dysphagia in IBM. Whilst VFSS is a commonly used technique in clinical practice; cumulative radiation exposure with repeated testing can be a limitation. Alternative imaging techniques could be developed further as outcome measures for assessing swallowing.

In this review, we provide an overview of imaging techniques used to assess swallowing and the insight provided from such investigations into the mechanisms behind dysphagia in IBM. We suggest future directions for evaluation and outcome measurement of dysphagia in this population.

Introduction

It is thought that between 40 and 80% of patients with IBM develop dysphagia at some stage (1-3). Swallowing difficulties in IBM patients are an under recognised problem (4). Dysphagia was previously considered to be a symptom of IBM that developed later on in the disease; however, it is now recognised as a presenting feature in a subset of patients (5-8). A retrospective study previously suggested that in 14% of IBM cases; dysphagia can be present for up to 10 years prior to limb muscle weakness developing (9). Alamr *et al*. recently described dysphagia as the most common atypical presentation, accounting for 50% of atypical presentations (7). Dysphagia is a major source of morbidity and mortality, resulting in complications such as aspiration pneumonia and malnutrition (1, 2, 10). There is evidence to suggest that the dysphagia observed in IBM is more prevalent and pronounced compared to other idiopathic inflammatory myopathies (IIMs) (3, 11).

The most common symptoms of dysphagia reported by IBM patients include repeated swallows and 'food getting stuck' in the throat. Asking about these symptoms could be a useful way to evaluate presence or absence of dysphagia in IBM (12). Other patient complaints include nasal regurgitation, coughing and choking (12, 13).

In some patients, dysphagia is the most prominent symptom and cause for severe morbidity. Taira *et al*. suggest that dysphagic IBM patients may display an altered pattern of limb weakness (14). Some reports indicate that dysphagia may be more prominent in women (12, 15, 16). Our group have highlighted a

subset of patients (all middle-aged females) presenting with early onset facial weakness and bulbar dysfunction, accompanied by marked respiratory failure requiring non-invasive ventilation (17). Further identification and characterisation of this phenotype is required. Another rare and recently described feature in IBM observed in the context of dysphagia is the presence of macroglossia (17, 18). However, further surveillance for macroglossia is required.

In general, the literature on dysphagia in IBM is heterogenous and of limited quality (10, 19). Most is limited to small cases studies, broader investigations into dysphagia with other IIMs and duplicated data (10, 19). Patient-reported outcomes specific to IBM such as the IBM Functional Rating Scale (IBMFRS) and sporadic IBM Physical Functioning Assessment (sIFA), incorporate only one or two items relevant to dysphagia (19). Before treatments can be accurately assessed, robust strategies need to be developed for monitoring dysphagia in IBM.

The aim of this review is to provide an overview on imaging techniques used to evaluate dysphagia in IBM and discuss the insight into pathogenesis gained from these techniques. We also outline future directions for visualising the anatomy and physiology of swallowing that could serve as potential biomarkers.

Pathophysiology of dysphagia in IBM

Over the last decade assays have been developed to detect antibodies against cytosolic 5'-nucleosidase 1A (cN1A) in IBM patients. The sensitivity for anti-cN1A antibodies ranges between 30-89% depending on the assay used.(20) Seropositivity has been associated with an increased mortality risk (21). Importantly, some reports suggest that seropositivity has been associated with increased risk of dysphagia (22, 23). The pathogenicity of anti-cN1A antibodies is yet to be determined. Immunisation of mice with cN1A peptides has generated anti-cN1A antibodies *de novo* and replicated some features of IBM (24). These mice lost weight, and this drop in weight could be predominantly due to reduced muscle mass. However, no specific assessments of feeding were made to further characterise the weight loss.

Endomysial infiltration with lymphocytes is a histopathological hallmark for IBM. Interestingly, presence of endomysial inflammation on limb muscle histology from IBM patients has been shown to have a significant correlation with more severe dysphagia (25).

Previous reports have described histopathological changes of biopsies from head or neck muscles such as cricopharyngeus (CP), sternohyoid, omohyoid and sternocleidomastoid muscles (5, 26-30). These reports describe endomysial inflammation within these muscles (26-30). In addition, histological examination of such muscles demonstrated other features compatible with IBM such as presence of rimmed vacuoles, p62 inclusions, necrosis, cytochrome-c oxidase negative and regenerating fibres (26-30). Such histopathological changes support the hypothesis that the same disease process is occurring in the muscles involved in swallowing.

Swallowing is a complex physiological process reliant on voluntary and involuntary mechanisms, (Fig. 1) (31, 32). As demonstrated in Figure 1, weakness in a variety of muscle groups may to contribute to dysphagia in IBM patients such as facial, masticatory, tongue, palatal and pharyngeal muscles. However, it is important to determine which muscles are principally responsible for dysphagia in IBM and if there is a specific pattern of bulbar muscle weakness. This would have implications for surveillance and determining appropriate treatment strategies. Deficits in the oral and pharyngeal phases of swallow appear to be the leading cause of dysphagia in IBM patients (Fig. 1) (4). Within that, upper oesophageal sphincter (UES) dysfunction is often described as a key biomechanical component (4, 13). The UES itself is composed of the inferior pharyngeal constrictor, CP and superior oesophagus (31). Opening of the UES is an important step in the pharyngeal phase of swallowing, enabling the food bolus to enter the oesophagus. Three key steps are required in UES opening. Firstly, reflex mediated relaxation of the CP muscle, which is tonically contracted at rest due to vagal stimulation (31, 32). Secondly, contraction of the suprahyoid and thyrohyoid muscles allowing hyolaryngeal elevation, the forward movement of which mechanically opens the UES (32). Finally, superior pressure from the food bolus contributes to UES opening. Impaired relaxation or opening of the UES leads to food stasis in areas such as the piriform fossa and epiglottic vallecula (4, 13, 31). Some patients with severe dysphagia may retain the food bolus above the CP and attempt to cough it back up before swallowing again.

Structural pathology within or impaired CP relaxation could result in reduced UES opening. Ambrocio *et al*. performed a systematic review of the literature on dysphagia assessment and management in IBM (19). After quality control only 19 articles met their criteria and were included. The authors found CP dysfunction to be the most reported deficit in IBM patients across 63% of studies reviewed. The driver for CP dysfunction in IBM has not yet been determined. Prominent fibrosis within the CP of IBM patients has been described in the literature (26, 29). Despite the classic histopathological features of IBM observed within the CP (as described above), many reports describe hypertrophy of CP macroscopically (33-35). This contradicts the atrophy noted in the limb musculature of IBM patients. This hypertrophy, fibrosis or even inflammation of the CP may therefore limit opening of the UES. In addition to these structural abnormalities, the presence of abnormal CP propulsions or prominence often described as CP bars have been observed in IBM patients (Fig. 2) (36, 37).

However, some evidence indicates that CP relaxation is not overtly impaired in IBM (3, 16). It has been suggested that weak suprahyoid muscle contraction and subsequent inadequate hyolaryngeal elevation contributes to reduced UES opening (3, 16, 33). The prevalence of impaired laryngeal elevation has been reported as high as 40–50% in some studies (16, 33). Conversely, real-time

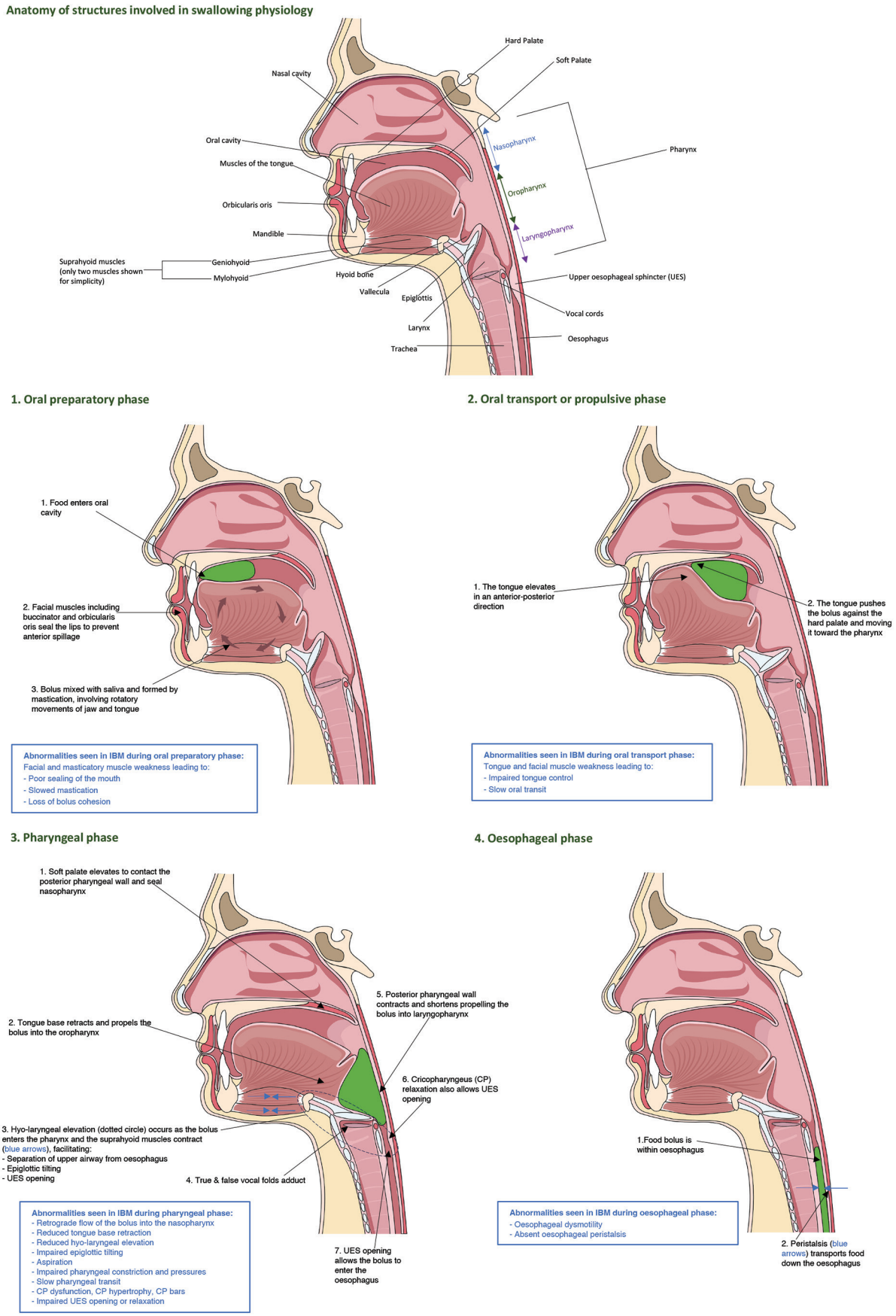

Fig. 1. Stages of swallowing and corresponding abnormalities in IBM. Illustration outlining the anatomical structures and normal physiological phases of swallowing. Sequential steps in the phases are numbered. Annotating boxes in blue represent some deficits observed in IBM to the corresponding phase.

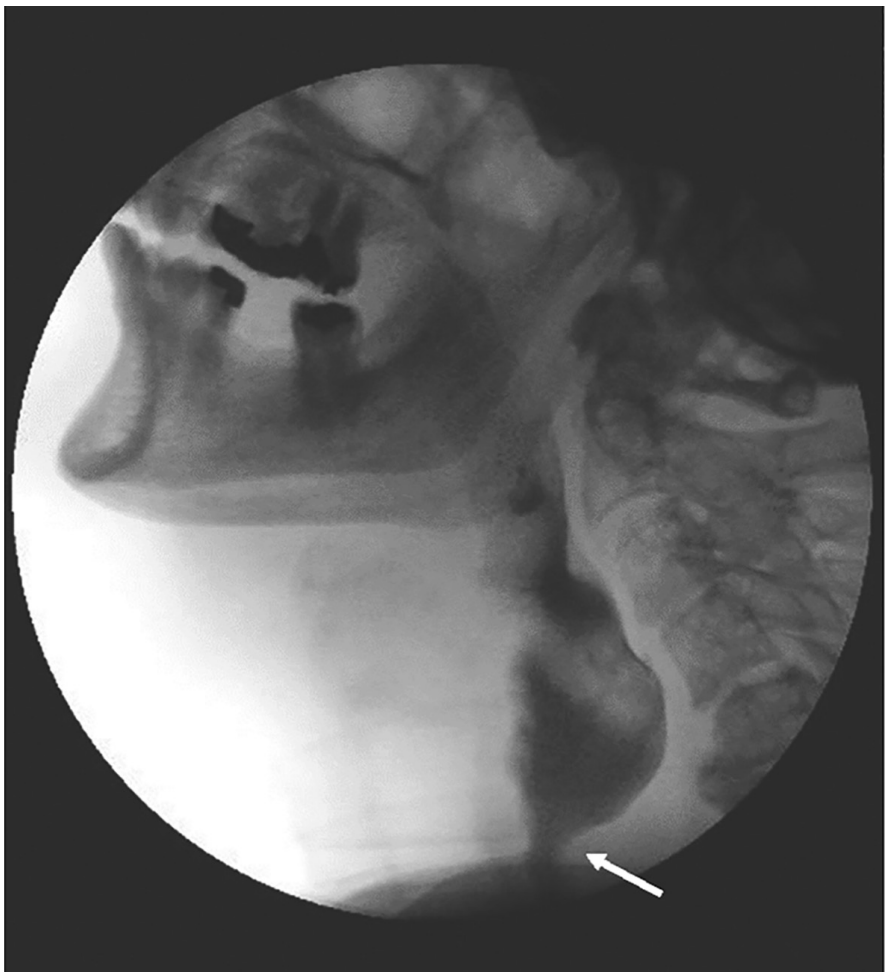

Fig. 2. Videofluoroscopic swallowing study (VFFS) image of a 73-year-old male with IBM, demonstrating prominence of the cricopharyngeal (CP) muscle during swallowing (shown by annotated arrow).

MRI (RT-MRI) performed in 20 IBM patients demonstrated mean laryngeal elevation to be within normal limits (36).

It is important to note that despite the significant emphasis on CP abnormalities and UES opening, other upstream mechanisms may contribute to oropharyngeal dysphagia in IBM and require more investigation. Slower mastication of food and prolonged oral transit in IBM patients has been described (36, 38). The presence of facial weakness in IBM has recently been shown to be associated with poorer Swallowing Quality of Life Questionnaire (SWAL-QOL) scores (39). Facial weakness leading to lip closure may impair the oral phases of swallow.(31) Impaired muscle contraction within the pharyngeal wall and reduced pharyngeal propulsion has been documented (12, 16, 33, 40, 41). Not only does this result in reduced bolus transit, but the lower pressure exerted from abnormal pharyngeal contraction may limit UES opening (13, 31). Deficits in tongue function, such as reduced base retraction and impaired tongue control have been noted in IBM (16, 33). Such deficits in the pharynx and tongue may lead to stasis within the oral cavity, difficulty initiating swallow, retention in the pharynx (again in piriform sinus and vallecula), impaired bolus propulsion and inadequate airway protection (31, 32).

Treating dysphagia in IBM

There are no validated treatments for IBM and specifically for swallowing impairments in IBM.

The study of behavioural interventions has been limited to small pilot studies or case reports of interventions such as lingual strengthening and expiratory manual strength training (EMST) (42, 43). Unfortunately, recent drug trials involving arimoclomol and biragrumab were unable to meet their primary endpoints (44, 45). Swallowing efficiency, measured by VFSS, did not differ between biragrumab and placebo, and swallowing-specific outcomes measures were not collected in the arimoclomol trial.

One pharmacological intervention for dysphagia that has been studied and often used in clinical practice is intravenous immunoglobulin (IVIG) (46-50). Associations between anti-cN1A seropositivity and presence of endomysial inflammation with dysphagia, lends some rationale for immunomodulation (22, 25). A small case series has evaluated the use of subcutaneous immunoglobulin reporting short lived benefits up to 1 year (51). There has only been one randomised controlled trial for IVIG in 19 patients (46). Although some benefit in swallowing was noted this trial had several limitations including sample size, risk of bias and a lack in description of swallowing deficits at baseline (52). Use of immunosuppressants such as azathioprine or mycophenolate have not demonstrated any clear efficacy in treating dysphagia (53).

Injection of botulinum into the CP has been limited to small studies and case reports (16, 54-56). The results from these studies have been variable, with the beneficial effect often being reversible. Treatment with balloon dilatation alone has been investigated in small case studies retrospectively, but the benefits have typically been transient lasting for a few weeks to several months (16, 35, 57).

The most commonly reported surgical technique is CP myotomy, usually within the context of case reports and small case studies, which describe variable benefits (5, 11, 16, 26-29, 38, 41, 58-60). The largest study of myotomy use in IBM to date was a retrospective review of transcervical and endoscopic myotomy in 41 IBM patients (59), where 12 patients demonstrated a statistically significant improvement according to patient-reported outcomes. It has been suggested that CP myotomy should only be performed if reduced UES relaxation is the key deficit and

Table I. Imaging techniques used to assess dysphagia in IBM and corresponding swallowing impairments. This table lists the techniques used in the literature to assess swallowing function in IBM and some of the abnormalities they have demonstrated. In addition, this table provides examples of measurements and scales that can be obtained from the imaging modalities listed.

Imaging technique	Measurements and scales	Findings observed in IBM patients
Videofluoroscopic Swallowing Studies (VFSS)	Oral transit time Pharyngeal transit time Upper oesophageal sphincter (UES) opening Laryngeal elevation Hyoid bone elevation Dynamic Imaging Grade of Swallowing (DIGEST) Penetration-Aspiration Scale (PAS) Modified Barium Swallow Impairment Profile (MBSImP) Analysis of Swallowing Physiology: Events, Kinematics and Timing (ASPEKT)	Impaired bolus control Prolonged oral transit time Impaired tongue control Impaired tongue base retraction Impaired pharyngeal contraction or constriction Pharyngeal pooling Prolonged pharyngeal transit time Impaired hyolaryngeal/laryngeal elevation Reduced epiglottic deflection or tilting Residue in vallecula and piriform fossa Cricopharyngeal enlargement Cricopharyngeal dysfunction Cricopharyngeal bars Impaired UES opening Aspiration Penetration Repeated swallows
Barium swallow	Structural evaluation of oesophagus Timed barium swallow - measurement of residual barium column above the oesophagogastric junction Oesophageal diameter	Appearance of cricopharyngeal tightness Cricopharyngeal prominence Oesophageal dysmotility
Flexible endoscopic evaluation of swallowing (FEES)	Structural evaluation of pharyngeal and laryngeal mucosa Penetration-Aspiration Scale (PAS) Yale Pharyngeal Residue Severity Rating Scale (YPRSRS)	Residue in vallecula and piriform fossa Aspitation Penetration
Manometry (pharyngoesophageal)	Intrabolus pressure Pharyngeal pressure (peak and nadir) Upper oesophageal sphincter (UES) resting pressure (peak and nadir) Lower oesophageal sphincter (LES) resting pressure	Low pharyngeal constriction pressure Reduced pharyngeal peristalsis Pharyngeal dysmotility High or normal UES relaxation pressure Reduced LES pressure Absence of oesophagus peristalsis
Real time MRI (RT-MRI)	Structural evaluation of pharynx, larynx, oesophagus Oral transit time Pharyngeal transit time Laryngeal elevation Extent of cricopharyngeus Oesophageal opening time	Prolonged oral transit time Prolonged pharyngeal transit time Cricopharyngeal bars Aspiration Penetration Prolonged oesophageal opening time

in the presence of normal hyolaryngeal elevation (3). Some small case studies have explored combined treatment regimens, such as balloon dilation combined with IVIG and botulinum injections, in addition to rehabilitation therapies (57, 61).

Often, feeding tubes, such as percutaneous endoscopic gastrostomy (PEG) tubes, are inserted for enteral feeding in patients with severe dysphagia.

In the majority of studies investigating interventions for dysphagia in IBM, small study populations were utilised, these studies were often retrospective, lacking randomisation and having no or poorly defined endpoints (10, 19, 52). Importantly, there is lack of investigation into the clinical outcomes specific to swallowing function in IBM, which could be reliably utilised to assess treatment responses (10, 19). Furthermore, better understanding of the pathophysiology may allow us to develop better targeted therapies.

Imaging swallowing impairments in IBM

Videofluoroscopic swallowing studies

Videofluoroscopic swallowing studies (VFSS) are a common approach to the assessment of oropharyngeal dysphagia in clinical and research settings, and is sometimes referred to as the modified barium swallow study (62). VFSS allow detailed dynamic assessment of the oral and pharyngeal phases of swallowing, plus screening of oesophageal function. The assessment takes 20-30 minutes, of which 3–4 minutes involve exposure to radiation. Patients receive boluses containing measured quantities of barium at different consistencies ranging from thin liquid to solids. Cumulative radiation exposure and the necessity for in-person hospital visits, especially in individuals who require regular follow up, are the main downsides to VFSS. Studies utilising VFSS in IBM often provide limited insight into the temporal resolution achieved,

one early report describes utilising 25 frames per second (fps) (19).

In an early study investigating IBM-related dysphagia, VFSS findings in 23 IBM patients were retrospectively assessed (16). The most frequent abnormalities seen were pharyngeal residue (91%), impaired tongue-base retraction (74%) and airway impaired penetration (70%). CP dysfunction (defined as prominent CP muscle with poor relaxation and narrowing in the upper oesophagus) was observed in 57% and aspiration was noted in 35%. 43% of patients had demonstrated impaired laryngeal elevation.

Cox *et al*. performed a prospective study characterising VFSS findings in 43 IBM patients, with 34 of which (79%) had abnormalities detected on VFSS (12). 56% had repeated swallowing, 44% had residues in the piriform sinus, 37% had residues in the vallecula, and 37% had CP dysfunction (posterior indentation of the CP).

Taira *et al*. retrospectively reviewed 45 IBM patients. The most frequent VFSS findings were impaired pharyngeal contraction (44%) and residue in the piriform sinus (44%) (14).

Recently, Shrivastava *et al*. retrospectively reviewed swallowing deficits in 24 IBM patients using VFSS (17/24) and barium swallow (7/24) (33). CP dysfunction (undefined by authors) and CP hypertrophy was observed in 75% (18/24). Impaired tongue base retraction was the most frequently abnormality reported, at 96%, followed by pharyngeal constrictor impairment in 92% and pharyngeal constrictor impairment in 82%. Reduced laryngeal elevation was seen in 50% of their cohort.

VFSS changes have been described in IBM patients asymptomatic of dysphagia, suggesting a degree of subclinical swallowing dysfunction (12, 40). Murata *et al*. performed VFSS and manometry in 10 IBM patients, 5 of whom reported no clinical symptoms of dysphagia. There was reduced pharyngeal propulsion in all IBM patients, although this was more severe in the dysphagic patients (40).

Presence of CP bars on VFSS

In recent years there has been interest in the relationship between the presence of CP bars on VFSS and dysphagia in IBM (14, 35-37, 63). This interest has peaked since the presence of abnormal CP propulsion has been described on RT-MRI (36). A CP bar is thought to represent impaired CP propulsion as consequence of abnormal pharyngeal contraction and impaired UES relaxation (37). CP bars may contribute to obstruction-related dysphagia within the pharynx. Taira *et al*. described an increased risk of aspiration in IBM patients when CP bars were detected on VFSS (37). Furthermore, the authors noted an association between the presence of CP bars in IBM patients and impaired UES opening. When comparing against other muscle disorders, the presence of a CP bar on VFSS showed a specificity of 96% for IBM (63). However the sensitivity was much lower at 33%. Patients with a CP bar were shown to have stronger knee extension and less fat infiltration within in the quadriceps muscle on MRI (14). These patients reported multiple swallow attempts and food getting caught in pharynx more frequently.(14) However, the utility of CP bars detected by VFSS is somewhat contentious as they can be seen in the presence of cervical osteophytes and in non-dysphagic elderly individuals (64). Further work is required to determine the value of CP bar detection in IBM.

Detecting aspiration on VFSS

Aspiration is often referenced as a major source of mortality and morbidity in IBM (1, 2). A recent systematic review noted aspiration in 47% (8/19) of articles reviewed (19). Aspiration was the second most commonly reported swallowing impairment, after CP dysfunction, and followed by the presence of residues. Of the studies reviewed for writing this manuscript, the rate of aspiration has been reported as high as 44% in dysphagic IBM patients by Schrey *et al*. (55). However, despite these observations, the presence of aspiration visible on VFSS is not universal. In the same study by Schrey *et al*., aspiration was not witnessed in any non-dysphagic IBM patients (55). Cox *et al*. described only one out of 43 patients demonstrating evidence of frank aspiration. However, the authors stated that 53% (23/43) patients displayed evidence of 'aspiration related signs' and 41% (18/43) had inadequate epiglottal downward tilting (12). Epiglottic tilting is a protective mechanism thought to help seal the laryngeal vestibule during swallowing, preventing aspiration (Fig. 1) (31). Similarly, in 2015 a retrospective review of 18 dysphagic IBM patients, revealed no aspiration visible on VFSS (35). Langdon *et al*. studied 18 IIM patients, including 8 IBM patients, using VFSS, and they described aspiration as an infrequent event (3). Four patients demonstrated aspiration, three of these patients had IBM. Murata *et al*. reported that all 10 patients they studied achieved a normal Penetration-Aspiration scale (PAS) score based on VFSS. (40) These discrepancies in the prevalence of aspiration may be attributed to a variety of factors, including study size, differing definitions of 'aspiration', and variation in the proportion of patients experiencing dysphagia within these study populations (13).

VFSS reporting tools

Reporting techniques used to describe VFSS impairments in IBM have been heterogenous and often descriptive in nature. Future investigations should use validated clinician-reported outcome tools for VFSS assessment. PAS is an eight-scale tool developed for VFSS (scores 1-2 are normal, scores 3-5 indicate penetration, and scores 6-8 indicate aspiration). PAS has been utilised in VFSS assessments of dysphagia in IBM, often in the context of evaluating responses to therapies in small case studies (33, 40, 43, 61). The Modified Barium Swallow Impairment Profile (MBSImP) allows the assessment of 15 physiological components across the three stages of swallow (62, 65). In addition, it allows assessment of oral and pharyngeal residue formation. While the use of MBSImP with VFSS has been validated, its application in IBM patients has not been studied in detail. A pilot study investigating the use of EMST to treat dysphagia in 10 patients, used the MBSImP as an outcome measure (43). Mean baseline MBSImP scores for regular boluses and thin bo-

luses, were 10 and 12 respectively. The recently developed Analysis of Swallowing Physiology: Events, Kinematics and Timing (ASPEKT) protocol; allows quantitative assessment of swallowing physiology (66). As further research is conducted in IBM, it is essential to employ validated approaches for reporting VFSS abnormalities.

- Barium swallow

Barium swallow is a radiographic procedure that predominantly assesses oesophageal structure and function (67). Only a few studies have described the use of barium swallow in IBM patients (16, 33). In an early study, barium swallow tests in 12 IBM patients where reviewed (34). There was evidence of CP prominence (42%) and reduced or absent peristalsis (42%). Oh *et al*. described the use of barium swallow in nine IBM patients, all of whom demonstrated a tight CP muscle (16). Shrivastava *et al*. reported barium swallow findings in conjunction with VFSS as described above (33). Barium swallows were reported to have a lower fps rate compared to VFSS (33). Barium swallows were retrospectively reviewed to assess swallowing function in IVIG or immunosuppressant-treated IBM patients; interestingly, oesophageal dysmotility was observed in 77% of patients (17/22) (48).

- Flexible endoscopic evaluation of swallowing

Flexible endoscopic evaluation of swallowing *(*FEES) is used to assess swallowing and upper airway function in clinical practice. A nasoendoscope is introduced via the nasal cavity to visualise the hypopharynx and larynx (4, 13). Food and liquids are also administered during visualisation. FEES is generally well tolerated, can be performed at bedside, and avoids radiation exposure. Validated scales have been developed for FEES reporting such as the Yale Pharyngeal Residue Severity Rating Scale (62). Unlike VFSS, FEES can evaluate secretions, laryngeal function and mucosa of the upper airways and pharynx. However, FEES doesn't allow detailed evaluation of the oral or oesophageal swallowing stages and biomechanical movements. In IBM patients artefact during FEES from 'white out' from residues hinder visualisation during the pharyngeal phase (13).

A limited number of studies have explored the use of FEES in IBM (16, 33, 36), with some offering only limited insights into the FEES phenotype of IBM patients. Two studies declare using temporal resolutions of 25 fps for FEES assessment of IBM patients (36, 43). Olthoff *et al*. compared the use of RT-MRI to VFSS and FEES in IBM (36). The detection of deficits such as retention and aspiration by FEES were comparable to VFSS. The degree of CP bar detection was inferior to VFSS and RT-MRI. A few small reports have utilised FEES assessments to measure responses to treatments such as EMST, Botox and endoscopic myotomy (43, 60, 61).

- Manometry

Another tool that has been used to investigate dysphagia in IBM patients is pharyngoesophageal manometry (3, 11, 16, 40, 68). It is primarily used to assess contraction of the pharyngeal muscles plus resting and relaxation pressures of the UES during oropharyngeal swallowing. It can be used together with other instrumental procedures such as VFSS (40, 69).

Oh *et al*. retrospectively reviewed 12 IBM patients who underwent pharyngoesophageal manometry (16). Details regarding the manometric technique and acquisition were not provided by the authors. Most patients had reduced pharyngeal contraction (75%) and reduced lower oesophageal sphincter (LES) pressures (42%). Interestingly, most patients studied demonstrated a normal UES relaxation and resting tone (82%).

As described above, Langdon *et al*. investigated dysphagia in 8 IBM patients (out of a total of 18 IIM patients) using manometry and VFSS (3). A manometry catheter (GutShop, Australia) was used, and data was computed at a sampling rate of 1 kHz. The authors found that, in general, pharyngeal pressures in patients were lower compared to normal ranges found in the literature. However, the authors concluded that UES relaxation pressures were not different from the ranges described in healthy individuals.

Murata *et al*. used computed pharyngoesophageal manometry using a 4-intraluminal pressure transducer assembly at four different sites (intranasally at oropharynx, hypopharynx, UES, and proximal oesophagus) (40). The sampling rate was not provided by the authors. UES relaxation and pressures were obtained whilst VFSS were performed. 10 IBM patients were recruited, five of whom reported dysphagia (40). In comparison to healthy controls, IBM patients generated lower pressures and reduced peristalsis within the oropharynx and hypopharynx (or laryngopharynx) (40). Unlike healthy individuals who demonstrate negative pressure during UES opening, this phenomenon was not observed in dysphagic IBM patients. Asymptomatic IBM patients also had evidence of impaired UES relaxation.

High resolution oesophageal manometry (HRM) has been implemented in clinical practice and research in recent years (70). A case report described the use of HRM in an IBM patient, revealing findings similar to those described by Murata *et al*. (40, 68). This patient demonstrated reduced pharyngeal pressures and elevated UES relaxation pressures.(68) Interestingly, reduced peristaltic activity within the oesophagus was observed, and LES pressure was in normal range.

Manometry has been used as an outcome measure in assessing various treatments of dysphagia in IBM in small case studies (51, 54, 57). Before utilising manometry measurements as an clinical outcomes for IBM these assessments need validating and their responsiveness evaluated (19). A common theme of impaired pharyngeal contraction and low pharyngeal pressures have been observed thus far. However, observations regarding UES relaxation have been more variable. Future studies with greater patient numbers are required to better characterise and obtain a consensus on the predominant manometric phenotype in IBM patients.

- Real-time MRI (RT-MRI)

RT- MRI is a novel technique that has been previously used to investigate swallowing function in healthy individ-

uals (71, 72). Olthoff *et al*. recruited 20 IBM patients who underwent RT-MRI, which is the first disease to be assessed by this technique.(36) Patients underwent VFSS, FEES, and other clinical assessments. 80% of the patients reported varying severities of dysphagia according to the SWAL-QOL (36). The scans were performed using a 3T MRI scanner (TimTrio, Siemens Healthcare) with the patients lying supine. The authors quote a true temporal resolution of 24.3 fps. Patients were given a 5 ml dose of pineapple juice with yeast as a contrast agent, with the manganese naturally present in this juice providing a high T1 signal. RT-MRI appeared to be a well-tolerated and safe despite boluses being given to patients whilst supine. In addition to morphological assessment of anatomy, RT-MRI allows quantification of transit times, including oral transit time (OTT), pharyngeal transit time (PTT), and oesophageal opening time (EOT). These times were all prolonged in IBM patients compared to healthy individuals (36, 71, 72).

Olthoff *et al*. described a 'CP propulsion' within the UES, visible on VFSS and RT-MRI but not in FEES. As previously discussed, it is thought that these CP propulsions are synonymous with CP bars (14, 36, 37, 63). No structural pathology within the oesophagus at rest on MRI could account for this phenomenon. CP bars was seen in 75% of patients, and the degree of CP bars was found to correlate with prolonged PTT.

Other studies have remarked on the importance of reduced hyolaryngeal elevation in dysphagic IBM patients (3, 16, 33). RT-MRI assessed laryngeal elevation more clearly than VFSS and FEES. RT-MRI demonstrated that mean laryngeal elevation did not have any significant associations with transit times, SWAL-QOL scores, and CP bar size. Furthermore laryngeal elevation did not appear to be abnormal in this IBM cohort, and mean laryngeal elevation was within normal limits. The authors suggested that these findings indicate that CP bars have a more significant role to dysphagia in IBM, compared with abnormal laryngeal elevation.

The degree of food retention present on RT-MRI was similar to VFSS. Bolus retention within the pharynx was reliably detected with VFSS, FEES and RT-MRI. Penetration detection was better assessed by VFSS or FEES compared to RT-MRI. The authors suggest this may be a result of a smaller bolus volume used in RT-MRI assessments.

This study did not include longitudinal assessments and had a relatively small sample size. Moreover, there were no age matched controls for more appropriate comparison to the IBM patients recruited to the study. Examining swallowing supine may lead to difficulties in deciphering between deficits secondary to IBM and compensatory effects from altered gravity. Finally, IBM patients tend to be elderly and may have medical contraindications to the performance of MRI.

Future directions for imaging dysphagia in IBM

Quantitative VFSS has been predominantly used a research tool and could an effective measure in IBM (73, 74). These techniques will aid in accurately measuring transit times and the degree of biomechanical movements including hyoid bone elevation. However, the issue of cumulative radiation exposure remains when monitoring patients in the long term.

Scintigraphy, a nuclear medicine technique, has shown validity in assessing oropharyngeal dysphagia (75). In a pilot trial using simvastatin to treat IBM, the investigators used oropharyngeal scintigraphy as a measure for dysphagia (76). However, only four patients in the study underwent scintigraphy, and no longitudinal changes were observed after treatment with simvastatin, although baseline deficits were not described in detail.

Various imaging techniques have been employed to visualise skeletal musculature in IBM (62). Some of these techniques could be applied to the assessment of swallowing muscles in IBM.

In the only randomised control trial of IVIG in IBM to date, the investigators employed ultrasound (US) to assess frequency of swallows but no information on structural abnormalities was provided (46). Quantitative US protocols have been developed to assess the bulbar muscles in neuromuscular diseases such as Duchenne's muscular dystrophy and oculopharyngeal muscular dystrophy (OPMD) (77-79). US of the bulbar muscle could assess the degree of intramuscular fat content based on echogenicity and muscle volume.

Another technique that could explore swallow function and determine the pattern of muscle involvement in IBM is quantitative MRI (qMRI). Our group have demonstrated that lower limb qMRI measurements such as fat fraction (FF) and remaining muscle area can be used monitor disease progression in IBM (80, 81). Similarly, qMRI techniques have been applied to assess bulbar musculature of Kennedy's disease and ALS patients (82). Klickovic *et al*. demonstrated that FF of the tongue musculature of Kennedy's disease patients to be significantly greater compared to healthy controls and ALS patients (82). The authors also described significant fat infiltration in palatal, masticatory and hyoid muscles using semi-quantitative techniques. qMRI has been used to explore the FF of tongue and masticatory muscles in OPMD patients (83, 84). Longitudinal increase in tongue muscle FF over 20 months was observed in OPMD patients (83). Baseline tongue FF correlated with functional measures such as isometric tongue pressure and maximum swallowing speed (83).

Conclusions

A large proportion of patients with IBM develop dysphagia at some stage in their disease course, albeit at differing levels of severity and patient impact. Clinicians should routinely screen for swallowing disturbances in clinic nuanced questioning, in particular screening questions for 'food getting stuck in the throat' and presence of 'repeated swallows' as outlined by Cox *et al*. (12). Although their validity in IBM needs evaluating, patient-reported questionnaires such as the dysphagia handicap index, Sydney swallowing questionnaire and SWAL-QOL, could be used to evaluate symptoms in more detail (19). We suggest proactive referral to dysphagia-specialist speech and language therapists experienced in neu-

romuscular disease, who will access instrumental evaluation judiciously, and provide information and education to facilitate patient self-monitoring and management. The timing of this referral may vary depending on other patient priorities, but as a general rule, we prefer early referral (85). Prior to considering invasive procedures altering CP anatomy in particular myotomy, it may be important to assess hyolaryngeal elevation in detail. The presence of markedly reduced hyolaryngeal elevation could limit the benefit of such interventions. Instrumental evaluation and standardised patient report outcome measures should be used to evaluate the impact of any surgical interventions to help build the evidence base for such procedures. We encourage early discussion regarding enteral tube feeding for patients suffering from rapidly progressive dysphagia affecting either nutrition, hydration, respiratory function or any of these issues combined.

Oropharyngeal dysphagia is thought to be the main factor contributing to impaired swallowing in IBM. While CP dysfunction is commonly described across various studies using different imaging modalities, functional deficits anatomically superior to the CP are also prevalent and likely play a significant role in dysphagic IBM patients. Pharyngeal abnormalities, such as impaired pharyngeal contraction and deficits in tongue function, have been reported at high rates in some studies. The precise mechanisms and pattern of muscle involvement behind swallowing dysfunction in IBM needs to be further elucidated. Better understanding of this pathophysiology will enable the development of targeted treatments and appropriate biomarkers. Imaging tools can provide insight into disease processes and objective assessments of treatment responses. VFSS is the most commonly used technique to assess dysphagia in IBM in clinical practice. Validated tools for VFSS have been developed but have not been specifically assessed in IBM. However, repeated radiation exposure from frequent VFSS assessments is a limitation. There is a need to further develop alternative imaging techniques to further elucidate the mechanism driving dysphagia in IBM and serve as clinical outcome measures in dysphagic IBM patients.

Competing interests

S. Salam is supported by the UCL Queen Square Institute of Neurology & Cleveland Clinic London MPhil/PhD Neuroscience Fellowship.

M.M. Dimachkie serves or has recently served as a consultant for Abata/Third Rock, Abcuro, Amicus, ArgenX, Astellas, Cabaletta Bio, Catalyst, CNSA, Covance/Labcorp, CSL-Behring, Dianthus, Horizon, EMD Serono/Merck, Ig Society, Inc, Janssen, Medlink, Octapharma, Priovant, Sanofi Genzyme, Shire Takeda, TACT/Treat NMD, UCB Biopharma, Valenza Bio and Wolters Kluwer Health/Up To Date. He has received research grants or contracts or educational grants from Alexion/Astra Zeneca, Alnylam Pharmaceuticals, Amicus, Argenx, Bristol-Myers Squibb, Catalyst, CSL-Behring, FDA/OOPD, GlaxoSmithKline, Genentech, Grifols, Mitsubishi Tanabe Pharma, MDA, NIH, Novartis, Octapharma, Orphazyme, Ra Pharma/UCB, Sanofi Genzyme, Sarepta Therapeutics, Shire Takeda, Spark Therapeutics, The Myositis Association and UCB Biopharma/RaPharma.

P.M. Machado has received honoraria from Abbvie, BMS, Celgene, Eli Lilly, Galapagos, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB.

The other authors have declared no competing interests.

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